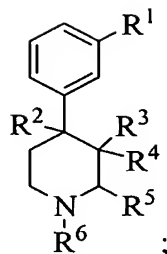


What is claimed:

1. A compound of formula I:



wherein:

$R^1$  is  $-OR^7$ ,  $-NR^7R^8$ ,  $-COOR^7$ ,  $-CONR^7R^8$ , or  $-CH_2OH$ ;

each  $R^7$  is independently H, alkyl, cycloalkyl, alkylcycloalkyl, or aralkyl;

each  $R^8$  is independently H, alkyl, aralkyl, or aryl;

$R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  are selected such that:

$R^2$  and  $R^5$  together form  $-(CH_2)_q-$ , where  $q$  is 2 to 4,  $R^3$  is alkyl, and  $R^4$  is H; or

$R^2$  and  $R^3$  together with the carbon atoms to which they are attached form a fused carbocycle,  $R^4$  is alkyl, and  $R^5$  is H;

$R^6$  is H or  $-(CHR^9)_mW$ ;

each  $R^9$  is independently H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl or heteroaryl;

$W$  is H, alkyl, cycloalkyl, alkylcycloalkyl, heterocycloalkyl, alkylheterocycloalkyl, aryl, heteroaryl,  $-CH_2OH$ ,  $-CH_2OR^7$ , or  $-C(=O)R^{10}$ ;

$R^{10}$  is  $-OR^7$  or  $-NR^7R^{11}$ ;

$R^{11}$  is H, alkyl, aralkyl, aryl or  $-(CHR^9)_n C(=O)R^{12}$ ;

$R^{12}$  is  $-OR^7$  or  $-NR^7R^8$ ;

$m$  is an integer from 1 to 4; and

$n$  is an integer from 1 to 4;

provided that when  $R^1$  is  $-OH$ , then  $W$  is heterocycloalkyl, alkylheterocycloalkyl,  $-CH_2OH$ , or  $-C(=O)R^{10}$ ; and when  $R^1$  is  $-OH$  and  $W$  is heterocycloalkyl or alkylheterocycloalkyl in which the heterocyclic ring moiety of the heterocycloalkyl or alkylheterocycloalkyl contains only one heteroatom, wherein the heteroatom is nitrogen, then the heterocyclic ring moiety is connected to  $-(CHR^9)_m-$  through a heterocyclic ring carbon atom;

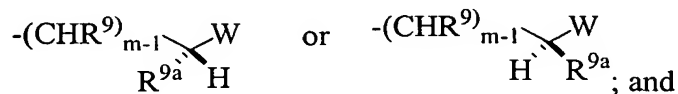
or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid hydrate, N-oxide or isomorphous crystalline form thereof.

2. A compound according to claim 1,  
wherein  $R^1$  is  $-OR^7$ ,  $-NR^7R^8$ , or  $-CONR^7R^8$ .

3. A compound according to claim 2,  
wherein  $R^1$  is  $-OH$ ,  $-NHR^8$ , or  $-CONHR^8$ .

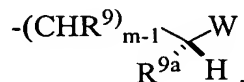
4. A compound according to claim 1,  
wherein  $R^6$  is  $-(CHR^9)_m W$ .

5. A compound according to claim 4,  
wherein:  
 $R^6$  is:

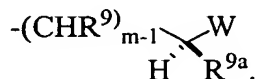


$R^{9a}$  is H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl or heteroaryl.

6. A compound according to claim 5,  
wherein:  
 $R^6$  is:

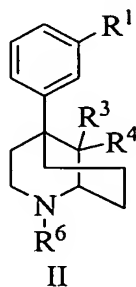


7. A compound according to claim 5,  
wherein:  
 $R^6$  is:

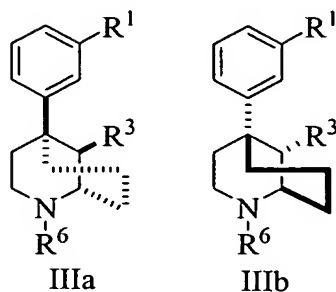


8. A compound according to claim 5,  
wherein W is aryl,  $-CH_2OH$ ,  $-CH_2OR^7$ , or  $-C(=O)R^{10}$ .

9. A compound according to claim 8,  
wherein W is aryl,  $-\text{CH}_2\text{OH}$ , or  $-\text{C}(=\text{O})\text{OH}$ .
10. A compound according to claim 8,  
wherein W is  $-\text{C}(=\text{O})\text{NR}^7\text{R}^{11}$ .
11. A compound according to claim 10,  
wherein W is  $-\text{C}(=\text{O})\text{NHR}^{11}$ .
12. A compound according to claim 11,  
wherein  $\text{R}^{11}$  is  $-(\text{CHR}^9)_n\text{C}(=\text{O})\text{R}^{12}$ .
13. A compound according to claim 12,  
wherein  $\text{R}^{11}$  is  $-(\text{CHR}^9)_n\text{C}(=\text{O})\text{OH}$ .
14. A compound according to claim 1,  
wherein m is 1 or 2.
15. A compound according to claim 1,  
wherein n is 1 or 2.
16. A compound according to claim 15,  
wherein n is 1.
17. A compound according to claim 1, of formula II:



18. A compound according to claim 17, of formula IIIa or IIIb:

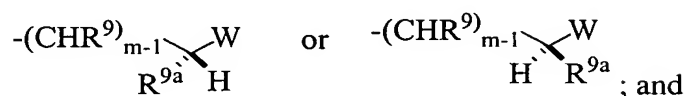


19. A compound according to claim 18, of formula IIIa.

20. A compound according to claim 18,  
wherein R<sup>3</sup> is methyl.

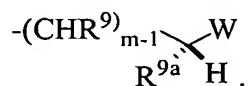
21. A compound according to claim 18,  
wherein R<sup>1</sup> is -OR<sup>7</sup>, -NR<sup>7</sup>R<sup>8</sup>, or -CONR<sup>7</sup>R<sup>8</sup>.

22. A compound according to claim 18,  
wherein:  
R<sup>6</sup> is:



R<sup>9a</sup> is H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl or heteroaryl.

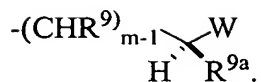
23. A compound according to claim 22,  
wherein:  
R<sup>6</sup> is:



24. A compound according to claim 23,  
wherein W is aryl, -CH<sub>2</sub>OH, or -C(=O)R<sup>10</sup>.

25. A compound according to claim 22,

wherein R<sup>6</sup> is:



26. A compound according to claim 25,  
wherein W is aryl, -CH<sub>2</sub>OH, or -C(=O)R<sup>10</sup>.

27. A compound according to claim 22,

wherein:

W is -C(=O)R<sup>10</sup>;

R<sup>10</sup> is -OR<sup>7</sup>;

R<sup>1</sup> is -NR<sup>7</sup>R<sup>8</sup>;

R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup> are each H;

R<sup>3</sup> is methyl;

R<sup>9a</sup> is benzyl; and

m is 2.

28. A compound according to claim 22,

wherein:

W is phenyl;

R<sup>1</sup> is -C(=O)NR<sup>7</sup>R<sup>8</sup>;

R<sup>3</sup> is methyl;

R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, and R<sup>9a</sup> are each H; and

m is 2.

29. A compound according to claim 23,

wherein:

W is -CH<sub>2</sub>OH;

R<sup>1</sup> is -NR<sup>7</sup>R<sup>8</sup>;

R<sup>3</sup> is methyl;

R<sup>7</sup> and R<sup>9</sup> are each H;

R<sup>8</sup> is -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>9a</sup> is benzyl; and

m is 2.

30. A compound according to claim 25,

wherein:

W is  $-\text{CH}_2\text{OH}$ ;

$\text{R}^1$  is  $-\text{NR}^7\text{R}^8$ ;

$\text{R}^3$  is methyl;

$\text{R}^7$  and  $\text{R}^9$  are each H;

$\text{R}^8$  is  $-\text{CH}_2\text{CH}_3$ ;

$\text{R}^{9a}$  is benzyl; and

m is 2.

31. A compound according to claim 25,

wherein:

$\text{R}^1$  is  $-\text{OR}^7$ ;

W is  $-\text{C}(=\text{O})\text{R}^{10}$ ;

$\text{R}^{10}$  is  $-\text{OR}^7$ ;

$\text{R}^3$  is methyl;

each  $\text{R}^7$  and  $\text{R}^9$  is H;

$\text{R}^{9a}$  is benzyl; and

m is 2.

32. A compound according to claim 25,

wherein:

$\text{R}^1$  and  $\text{R}^{12}$  are each  $-\text{OR}^7$ ;

W is  $-\text{C}(=\text{O})\text{R}^{10}$ ;

$\text{R}^{10}$  is  $-\text{NR}^7\text{R}^{11}$ ;

$\text{R}^3$  is methyl;

each  $\text{R}^7$  and  $\text{R}^9$  is H;

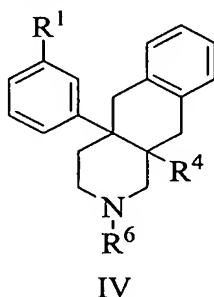
$\text{R}^{9a}$  is benzyl;

$\text{R}^{11}$  is  $-(\text{CHR}^9)_n\text{C}(=\text{O})\text{R}^{12}$ ;

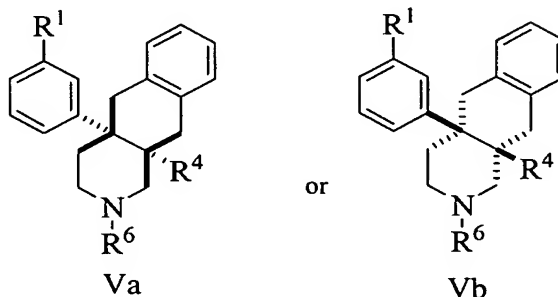
m is 2; and

n is 1.

33. A compound according to claim 1,  
wherein  $R^2$  and  $R^3$  together with the carbon atoms to which they are attached form a fused carbocycle.
34. A compound according to claim 33,  
wherein the fused carbocycle is tetrahydroindene, tetrahydronaphthalene, or tetrahydroanthracene.
35. A compound according to claim 34,  
wherein the fused carbocycle is tetrahydronaphthalene.
36. A compound according to claim 1, of formula IV:



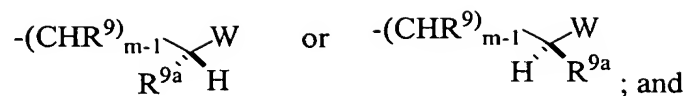
37. A compound according to claim 36, of formula Va or Vb:



38. A compound according to claim 37,  
wherein  $R^4$  is methyl.
39. A compound according to claim 38,

wherein:

R<sup>6</sup> is:

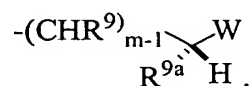


R<sup>9a</sup> is H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl or heteroaryl.

40. A compound according to claim 39,

wherein:

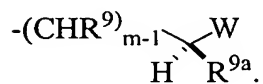
R<sup>6</sup> is:



41. A compound according to claim 39,

wherein:

R<sup>6</sup> is:



42. A compound according to claim 41, of formula Va,

wherein:

R<sup>1</sup> and R<sup>10</sup> are each -OR<sup>7</sup>;

R<sup>4</sup> is methyl;

R<sup>7</sup> and R<sup>9</sup> are each H;

R<sup>9a</sup> is benzyl;

W is -C(=O)R<sup>10</sup>; and

m is 2.

43. A compound according to claim 41, of formula Va,

wherein:

R<sup>1</sup> and R<sup>12</sup> are each -OR<sup>7</sup>;

R<sup>4</sup> is methyl;

R<sup>7</sup> and R<sup>9</sup> are each H;

R<sup>9a</sup> is benzyl;



W is  $-C(=O)R^{10}$ ;  
 $R^{10}$  is  $-NR^7R^{11}$ ;  
 $R^{11}$  is  $-(CHR^9)_n C(=O)R^{12}$ ;  
 n is 1; and  
 m is 2.

44. A compound according to claim 39, of formula Vb,

wherein:

$R^1$  is  $C(=O)NR^7R^8$ ;  
 $R^4$  is methyl;  
 $R^7$ ,  $R^8$ ,  $R^9$ , and  $R^{9a}$  are each H;  
 W is phenyl; and  
 m is 2.

45. A compound according to claim 1,

wherein the compound is:

2-benzyl-3-[5-(3-hydroxy-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-propionic acid;

{2-benzyl-3-[5-(3-hydroxy-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-propionylamino}acetic acid;

2-benzyl-3-[5-(3-ethylamino-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-propan-1-ol;

2-benzyl-3-[5-(3-ethylamino-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-propan-1-ol;

3-[5-(3-amino-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-2-benzyl-propionic acid;

3-[9-methyl-2-phenylethyl-2-aza-bicyclo[3.3.1]non-5-yl]-benzamide;

2-benzyl-3-[4a-(3-hydroxy-phenyl)-10a-methyl-3,4,4a,5,10,10a-hexahydro-1H-benzo[g]isoquinolin-2-yl]-propionic acid;

{2-benzyl-3-[4a-(3-hydroxy-phenyl)-10a-methyl-3,4,4a,5,10,10a-hexahydro-1H-benzo[g]isoquinolin-2-yl]-propionylamino}-acetic acid;

3-(10a-methyl-2-phenethyl-1,3,4,5,10,10a-hexahydro-2H-benzo[g]isoquinolin-4a-yl)-benzamide;

or stereoisomers thereof.

46. A compound according to claim 45,  
wherein the compound is:  
2(S)-benzyl-3-[5-(3-hydroxy-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-  
propionic acid;  
{2(S)-benzyl-3-[5-(3-hydroxy-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-  
propionylamino}acetic acid;  
2(S)-benzyl-3-[5-(3-ethylamino-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-  
propan-1-ol;  
2(R)-benzyl-3-[5-(3-ethylamino-phenyl)-9-methyl-2-aza-bicyclo[3.3.1]non-2-yl]-  
propan-1-ol;  
or partial stereoisomers thereof.
47. A pharmaceutical composition, comprising:  
a pharmaceutically acceptable carrier; and  
an effective amount of a compound according to claim 1.
48. A pharmaceutical composition according to claim 47,  
further comprising an effective amount of at least one opioid.
49. A pharmaceutical composition according to claim 48,  
wherein the opioid is alfentanil, buprenorphine, butorphanol, codeine, dezocine,  
dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine  
(pethidine), methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine,  
propiram, propoxyphene, sufentanil, tramadol or mixtures thereof.
50. A method of binding opioid receptors in a patient in need thereof, comprising the step of:  
administering to the patient a composition comprising an effective amount of a  
compound according to claim 1.
51. A method according to claim 50,  
wherein the compound binds  $\mu$  opioid receptors.

52. A method according to claim 51,  
wherein the  $\mu$  opioid receptors are located in the central nervous system.
53. A method according to claim 51,  
wherein the  $\mu$  opioid receptors are located peripherally to the central nervous system.
54. A method according to claim 50,  
wherein the compound binds  $\kappa$  opioid receptors.
55. A method according to claim 54,  
wherein the  $\kappa$  opioid receptors are located in the central nervous system.
56. A method according to claim 54,  
wherein the  $\kappa$  opioid receptors are located peripherally to the central nervous system.
57. A method according to claim 50,  
wherein the compound binds  $\delta$  opioid receptors.
58. A method according to claim 54,  
wherein the  $\delta$  opioid receptors are located in the central nervous system.
59. A method according to claim 54,  
wherein the  $\delta$  opioid receptors are located peripherally to the central nervous system.
57. A method according to claim 50,  
wherein the binding antagonizes the activity of the opioid receptors.
58. A method according to claim 50,

wherein the compound exhibits activity toward the opioid receptors.

59. A method according to claim 50,  
wherein the compound does not substantially cross the blood-brain barrier.
60. A method according to claim 50,  
wherein the patient is in need of prevention or treatment of a condition or disease caused by an opioid.
61. A method according to claim 60,  
wherein the opioid is endogenous.
62. A method according to claim 60,  
wherein the opioid is exogenous.
63. A method according to claim 60,  
wherein the composition further comprises an effective amount of at least one opioid.
64. A method of preventing or treating gastrointestinal dysfunction, comprising the step of:  
administering to a patient in need thereof, a composition comprising an effective amount of a compound according to claim 1.
65. A method of preventing or treating ileus, comprising the step of:  
administering to a patient in need thereof, a composition comprising an effective amount of a compound according to claim 1.
66. The method of claim 65,  
wherein the ileus is post-operative ileus.
67. A method of preventing or treating obesity, comprising the step of:  
administering to a patient in need thereof, a composition comprising an effective amount of a compound according to claim 1.

68. A method of preventing or treating a side effect associated with an opioid, comprising the step of:  
administering to a patient in need thereof, a composition comprising an effective amount of a compound according to claim 1.
69. A method according to claim 68,  
wherein the side effect is selected from the group consisting of constipation, nausea, vomiting, and combinations thereof.
70. A method according to claim 68,  
wherein the administering step occurs before, during or after a step of administering at least one opioid.
71. A method according to claim 70,  
wherein the opioid is alfentanil, buprenorphine, butorphanol, codeine, dezocine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine (pethidine), methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propiram, propoxyphene, sufentanil, tramadol or mixtures thereof.
72. A method of preventing or treating pain, comprising the step of:  
administering to a patient in need thereof, a composition comprising:  
an effective amount of an opioid; and  
an effective amount of a compound according to claim 1.
73. A method according to claim 72,  
wherein the opioid is alfentanil, buprenorphine, butorphanol, codeine, dezocine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine (pethidine), methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propiram, propoxyphene, sufentanil, tramadol or mixtures thereof.